Urological Science 25 (2014) 91–94

Contents lists available at ScienceDirect

Urological Science

journal homepage: www.urol-sci.com

Case report

# Paraganglioma of the urinary bladder with pelvic metastasis

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ARTICLE INFO

*Article history:*
Received 2 January 2013
Received in revised form
6 March 2013
Accepted 27 May 2013
Available online 19 August 2013

*Keywords:*
bladder paraganglioma
bladder tumors
extra-adrenal pheochromocytoma

ABSTRACT

A 52-year-old male, diagnosed with paraganglioma of the urinary bladder, underwent transurethral resection of the bladder tumor 10 years ago. He was lost to follow-up after the operation but was recently admitted to our hospital for the treatment of nasopharyngeal cancer. However, refractory hypertension with palpitation was noted and a computed tomography scan revealed a round, well-defined mass at the right pelvic region. Retroperitoneal tumor excision surgery was performed and a subsequent pathological analysis revealed paraganglioma. The diagnosis of paraganglioma of the urinary bladder with pelvic metastasis was confirmed and his blood pressure returned to normal level without medication after the operation.


## 1. Introduction

Catecholamine-secreting tumors that arise from chromaffin cells of the adrenal medulla and the sympathetic ganglia are referred to as pheochromocytomas and catecholamine-secreting paragangliomas (extra-adrenal pheochromocytomas), respectively. Approximately 10% of pheochromocytomas originate from extra-adrenal organs, primarily from para-aortic sympathetics. Bladder pheochromocytoma is a rare neoplasm accounting for less than 1% of all pheochromocytomas[1] and less than 0.06% of all bladder tumors.[2] The bladder pheochromocytomas usually arise from submucosal or muscularis propria and not from perivesical tissue and they are most common in the trigone region.[3] Malignant pheochromocytomas are histologically and biochemically the same as benign ones. The only reliable clue to the presence of a malignant pheochromocytoma is local invasion or distant metastases, which may occur as long as 20 years after a resection. We herein present a case of bladder paraganglioma with pelvic metastasis and discuss the clinical, image, and surgical findings.

## 2. Case report

A 52-year-old male had painless gross hematuria for days and he also mentioned urination with palpitation and headache for 2 years. He denied any history of hypertension or arrhythmia. An abdominal echo showed a bladder tumor over the right side of the urinary bladder. Cystoscopy revealed a submucosal protruding mass (Fig. 1A) and transurethral resection (TUR) of the bladder tumor was done on February 7, 2002. A pathological analysis confirmed paraganglioma. 123-I-metaiodobenzylguanidine (MIBG) scintigraphy was done and the results showed low probability of distant metastases (Fig. 1B). He was lost to follow-up in our outpatient department after the operation.

On February 3, 2012, he was admitted to our hospital for the treatment of nasopharyngeal cancer. However, refractory hypertension as high as 170–190 mmHg (systolic blood pressure) with palpitation was noted. Abdominal computed tomography (CT) was arranged and a 4.2 cm × 3.9 cm × 4.0 cm round, well-defined mass at the right pelvic region beside the urinary bladder (Fig. 2) was found. The 24-hour urine vanillylmandelic acid (VMA; 15.67 mg/day) was administered (normal range: 1–7.5 mg/day).

He was transferred to our urologic ward and an oral form of alpha blocker, terazosin hydrochloride (Hytrin), was administrated for 1 week prior to the operation. Then, retroperitoneal tumor excision surgery was performed on February 13, 2012. Fluctuating blood pressure (systolic blood pressure as high as 230 mmHg) was noted perioperatively, and sodium nitroprusside was administrated. However, it had poor response and perdipine (nicardipine) pump, a short-acting calcium-channel blocker, was used to control the blood pressure. We ceased surgery several times until the systolic blood pressure returned to normal level and the tumor was

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1879-5226 
http://dx.doi.org/10.1016/j.urols.2013.05.013

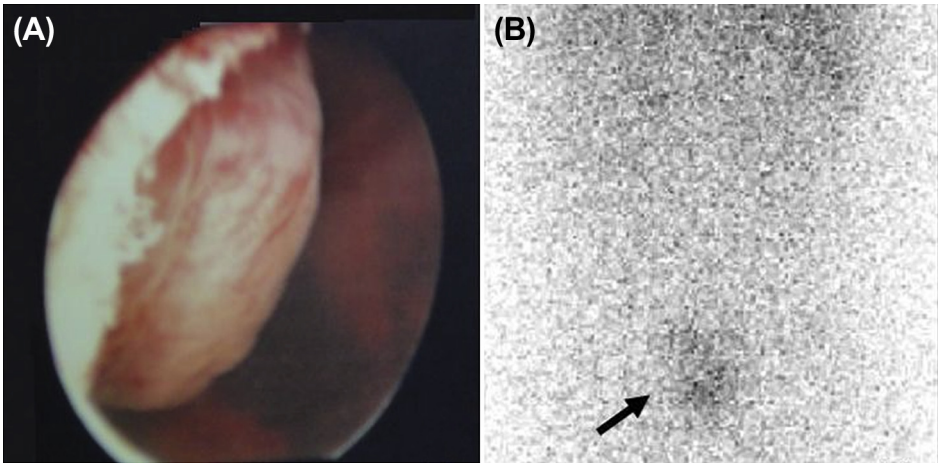


**Fig. 1.** (A) Cystoscopy showed a hypervascular, protruding mass over the right lateral wall of the urinary bladder. (B) $I^{131}$-MIBG revealed a high uptake at the urinary bladder and low probability of distant metastases. MIBG = metaiodobenzylguanidine.

finally removed smoothly (Fig. 3A and B). A pathological analysis of the isolated tumor confirmed paraganglioma (Fig. 3C and D). After the operation, the blood pressure became normal without medication and the patient was discharged uneventfully.

## 3. Discussion

Paraganglioma of the urinary bladder is a rare disease and accounts for 10% of extra-adrenal pheochromocytoma. The clinical presentation of paraganglinoma of the bladder is painless hematuria (50–60%), hypertension (65–80%), headache, and palpitation during micturition.[3] The average age at diagnosis is the $4^{th}$–$5^{th}$ decade and has an incidence of approximately 1:3 in men and women. Malignant pheochromocytomas are defined as tumors with local invasion or distant metastases. These tumors account for 10% of all pheochromocytomas. However, extra-adrenal pheochromocytomas are malignant in 29–40% of cases.[4,5] Thus, extra-adrenal pheochromocytomas might have a higher malignant potential than adrenal pheochromocytomas. For this reason, long-term follow-up should be recommended in patients with extra-adrenal pheochromocytoma.[6,7]

The diagnostic tests for paraganglioma of the urinary bladder include 24-hour urine or plasma fractionated catecholamines and metanephrines. Because bladder paragangliomas sometimes lack converting enzymes called phenylethanolamine *N*-methyltransferase, elevated norepinephrine levels can be found.[8] Imaging

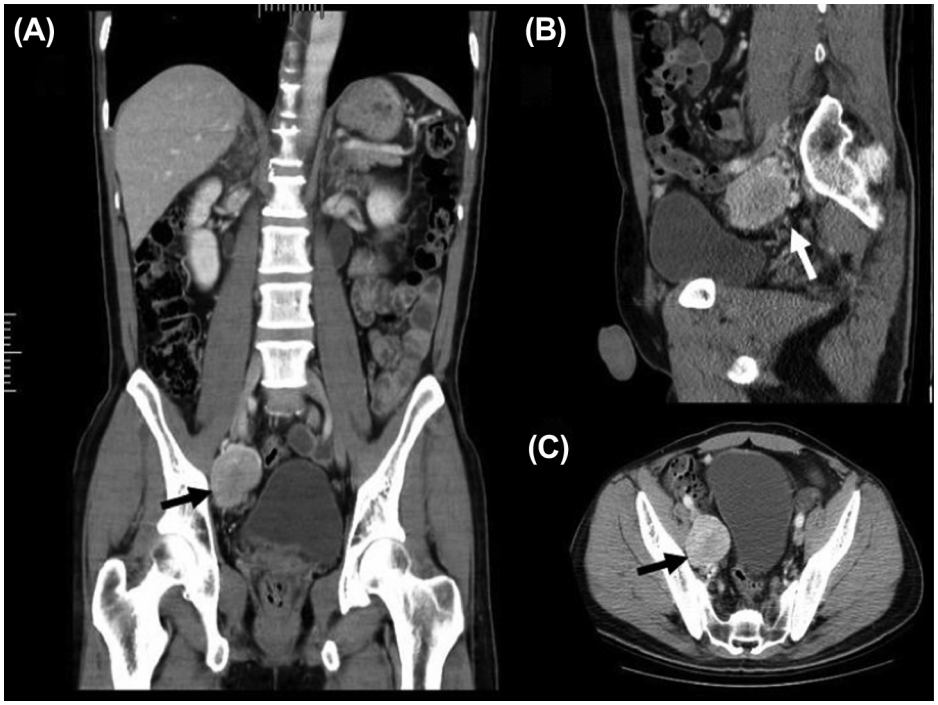


**Fig. 2.** Biphasic computed tomography revealed a 4.2 cm × 3.9 cm × 4.0 cm round, well-defined and enhanced mass at the right pelvic region beside the urinary bladder (arrow): (A) coronal view; (B) sagittal view; (C) transverse view. There was no connection between them.

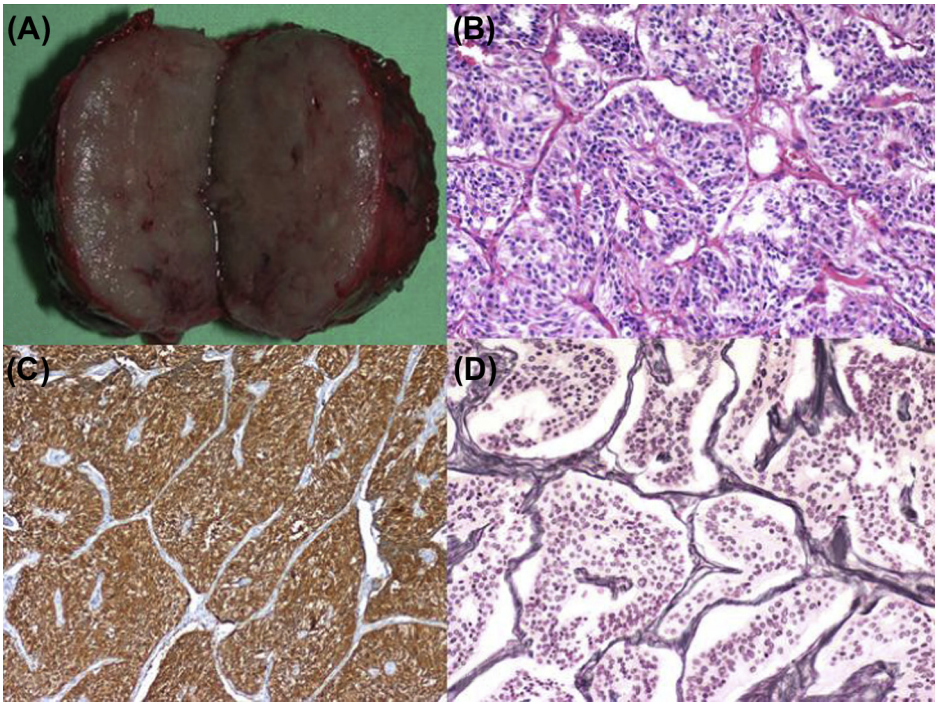


**Fig. 3.** (A) Macroscopic appearance revealed an encapsulated solid tumor with gray to tan cut surface without necrosis. (B) The tumor cells are round with acidophilic granular cytoplasm and ovoid nuclei with fine granular chromatin, arranged in discrete nests (the zellballen pattern) separated by a prominent vascular network (hematoxylin–eosin, 200×). (C) These tumor cells are positive for NSE, chromogranin, and synaptophysin staining (NSE, 100×). (D) These cells were arranged in zellballen pattern or the nests are separated by silver-positive fibrous septum (S-100, 100×). NSE = neuron-specific enolase.

studies, ultrasonography, CT, magnetic resonance imaging (MRI), and $I^{131}$-MIBG can provide more detail about the tumor. On ultrasonography, bladder paragangliomas are seen as heterogenous, hypoechoic, and well-defined lesions, but differential diagnosis cannot be made vis-à-vis other bladder tumors. Biphasic CT shows homogeneous hyperenhanced soft-tissue mass. MRI is superior to CT for the demonstration of the submucosal tumor and has a higher sensitivity (88%).[9] Bladder paragangliomas are typically hypointense on T1-weighted images and exhibit hyperintensity on T2-weighted images. Ring calcification around the circumference of the mass is another highly suggestive characteristic.

Although MRI and CT scanning provide fine anatomical details in locating these tumors, only the use of $I^{131}$-MIBG allows easy, cost-effective, whole-body scanning to help localize this catecholamine-producing tumor. On cystography, such tumors appear granulated and lobulated, protruding into the bladder as globular yellowish, submucosal tumors. Irrigating the mass during cystoscopy can be helpful in confirming the diagnosis preoperatively as the blood pressure fluctuates. Cystoscopic biopsies are usually not advocated because positive rate is very low, they bleed easily, and can induce blood pressure fluctuation.[7]

The treatments of bladder pheochromocytomas are partial cystectomy (open or laparoscopic), total cystectomy, and TUR. However, if distant metastases are found, complete resection of the metastatic tumors is recommended. If complete radical resection is not available, arterial embolization, cryoablation, chemotherapy, and MIBG radiation therapy can be considered.[10] A retrospective report revealed that systemic chemotherapy with cyclophosphamide, vincristine, and dacarbazine had a tumor response rate of 55% and a biochemical response rate of 72%.[11]

Our patient had bladder paraganglioma status post-TUR, which was performed 10 years ago, and refractory hypertension was noted recently. A metastatic pelvic mass was noted on CT scan and no recurrent bladder tumor was found. Elevated 24-hour urine VMA confirmed the diagnosis. Complete resection of the pelvic mass was performed and a pathological analysis confirmed paraganglioma. The patient's blood pressure returned to normal without receiving any antihypertensive medication after the operation and repeated close follow-up with indefinite annual biochemical/imaging screening is recommended for such patients.

In conclusion, bladder paraganglioma with pelvic metastasis is a rare condition, and such rarity limits proper development of therapies. Complete resection is thought to be the best policy, but if complete resection cannot be done, alternative treatment should be considered. Further studies in patients receiving surgery or other therapies are necessary to establish a standard for the disease.

## Conflicts of interest

The authors declare that they have no financial or non-financial conflicts of interest related to the subject matter or materials discussed in the manuscript.

## Source of funding

None.

## References

1. Melicow MM. One hundred cases of pheochromocytoma (107 tumors) at the Columbia-Presbyterian Medical Center, 1926–1976: a clinicopathological analysis. *Cancer* 1977;**40**:1987–2004.
2. Leestma JE, Price Jr EB. Paraganglioma of the urinary bladder. *Cancer* 1971;**28**:1063–73.
3. Ansari MS, Goel A, Goel S, Durairajan LN, Seth A. Malignant paraganglioma of the urinary bladder. A case report. *Int Urol Nephrol* 2001;**33**:343–5.

4. van Heerden JA, Sheps SG, Hamberger B, Sheedy 2nd PF, Poston JG, ReMine WH. Pheochromocytoma: current status and changing trends. *Surgery* 1982;**91**:367–73.
5. Scott Jr HW, Halter SA. Oncologic aspects of pheochromocytoma: the importance of follow-up. *Surgery* 1984;**96**:1061–6.
6. Kurosaka S, Irie A, Ishii J, Minei S, Takasima R, Kadowaki K, et al. Primary symptomatic perivesical paraganglioma: a case report. *Hinyokika Kiyo* 2007;**53**:903–6.
7. Vyas S, Kalra N, Singh SK, Agarwal MM, Mandal AK, Khandelwal N. Pheochromocytoma of urinary bladder. *Indian J Nephrol* 2011;**21**:198–200.
8. Eisenhofer G, Huynh TT, Pacak K, Brouwers FM, Walther MM, Linehan WM, et al. Distinct gene expression profiles in norepinephrine- and epinephrine-producing hereditary and sporadic pheochromocytomas: activation of hypoxia-driven angiogenic pathways in von Hippel–Lindau syndrome. *Endocr Relat Cancer* 2004;**11**:897–911.
9. Jalil ND, Pattou FN, Combemale F, Chapuis Y, Henry JF, Peix JL, et al. Effectiveness and limits of preoperative imaging studies for the localisation of pheochromocytomas and paragangliomas: a review of 282 cases. French Association of Surgery (AFC), and The French Association of Endocrine Surgeons (AFCE). *Eur J Surg* 1998;**164**:23–8.
10. Eisenhofer G, Bornstein SR, Brouwers FM, Cheung NK, Dahia PL, de Krijger RR, et al. Malignant pheochromocytoma: current status and initiatives for future progress. *Endocr Relat Cancer* 2004;**11**:423–36.
11. Huang H, Abraham J, Hung E, Averbuch S, Merino M, Steinberg SM, et al. Treatment of malignant pheochromocytoma/paraganglioma with cyclophosphamide, vincristine, and dacarbazine: recommendation from a 22-year follow-up of 18 patients. *Cancer* 2008;**113**:2020–8.